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Editorial

Charting the Future of Cancer and Organ Failure Care: A New Forum for Oncology, Nuclear Medicine and Transplantology

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Abstract:
This inaugural editorial introduces the new journal, "Oncology, Nuclear Medicine and Transplantology," launched by the National Research Oncology Center (NROC) in Kazakhstan. It outlines the journal's mission to serve as a pivotal interdisciplinary platform integrating these three rapidly evolving and interconnected fields. The editorial emphasizes the journal's commitment to addressing significant healthcare challenges at the national level in Kazakhstan, stimulating regional collaboration across Central Asia, and contributing to the global scientific discourse. The goal is to foster the exchange of original research, clinical experiences, and innovative practices to ultimately improve patient care and advance medical science in these critical specialties.

Keywords: Oncology; Nuclear Medicine; Transplantology; Kazakhstan

A Welcome from the Editor-in-Cheif

It is with immense pride and a profound sense of responsibility that I welcome you to the inaugural issue of the journal ***"Oncology, Nuclear Medicine and Transplantology."*** Launched under the auspices of the National Research Oncology Center (NROC), this journal represents a pivotal step in our collective mission to advance medical science and improve patient outcomes. Our primary goal is to create a dynamic, interdisciplinary forum where groundbreaking research translates into tangible clinical progress.

The establishment of this journal is a strategic response to the evolving landscape of modern medicine. The boundaries between oncology, nuclear medicine, and transplantology are increasingly blurring, giving rise to powerful, integrated approaches to complex diseases [1]. This publication is founded on the conviction that the synergy of these specialties is essential for tackling the healthcare challenges of our time.

Addressing National Priorities in Kazakhstan

In Kazakhstan, the burden of cancer and organ failure represents a significant challenge to our healthcare system [2, 3]. The National Research Oncology Center stands as a beacon of progress, embodying our nation's commitment to combating these diseases through innovation. The deployment of cutting-edge technologies—such as proton therapy, advanced radionuclide treatments, and molecular genetic diagnostics—has positioned NROC as a national reference center [4, 5]. This journal will serve as a crucial platform to disseminate these advancements across Kazakhstan, fostering a unified standard of excellence and supporting the continuous professional development of our medical community. It is a testament to our national resolve to not only adopt global standards but to contribute meaningfully to them

A Catalyst for Regional Advancement in Central Asia

The challenges we face in Kazakhstan are shared across Central Asia. Issues of access to advanced diagnostics, specialized surgical care, and novel therapeutics are common [6]. There is a pressing need for a regional platform that facilitates the exchange of knowledge, clinical experiences, and research findings specific to our demographic and epidemiological context. ***"Oncology, Nuclear Medicine and Transplantology"*** aims to be that catalyst. By highlighting regional research on cancer epidemiology, the practical application of nuclear medicine in resource-conscious settings, and the development of sustainable transplant programs—including vital areas like bone marrow, liver, and kidney transplantation [7]—we hope to accelerate progress and build collaborative networks across Central Asia. Strengthening regional expertise is key to improving healthcare outcomes for millions.

Engaging with Global Scientific Discourse

On a global scale, medicine is navigating an era of unprecedented change. The rise in cancer incidence, the promise of personalized therapy, the revolution in radiopharmaceuticals for both diagnostics and treatment (theranostics) [8, 9], and the remarkable innovations in transplant immunology are defining the future of patient care [10]. To make a meaningful impact, we must engage actively in the worldwide scientific conversation. This journal is our invitation to that dialogue. We are committed to publishing high-quality, original research, insightful reviews, and challenging clinical cases that meet international standards. We especially encourage submissions that explore the intersection of our core fields—for instance, the role of PET/CT in staging for transplant eligibility, or the use of radionuclide therapy as a bridge to transplantation.

Our mission is to build a bridge between scientists and clinicians in the CIS region and the international community. We are open to researchers from all corners of the world and believe that the diversity of perspectives enriches scientific discovery. True innovation is born from partnership.

Acknowledgement and a Look Forward

On behalf of the Editorial Board, I extend my deepest gratitude to the authors, reviewers, and dedicated colleagues whose unwavering support and expertise have brought this vision to life. Launching a new journal is an endeavor built on collective faith and effort.

We are confident that, through our shared commitment, ***"Oncology, Nuclear Medicine and Transplantology"*** will grow into a respected and influential publication—a platform where new ideas are ignited, and new horizons in patient care are forged. We invite you to read, submit, critique, and collaborate.

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Review Article

Evaluation of the Efficiency of the Admission Department in the Oncological Hospital using the Example of NROC

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Abstract:

Introduction: This study is aimed at assessing the operational efficiency of the admission department of the National Research Oncological Center (NROC) for the period from 2020 to 2024 with an emphasis on the impact of digitalization on patient management and workflow optimization. Telemedicine is a key tool for improving the availability and quality of medical care, especially for patients living in remote regions. In oncology, its importance is increasing due to the need for interdisciplinary interaction and quick routing of patients.

Methods: A retrospective analysis was conducted using internal hospital records, admission logs, and national healthcare regulations. Key performance indicators were assessed, including patient intake volume, processing time, and rejection rates. The impact of digital tools such as automated registration, routing algorithms, and remote clinical validation was examined.

Results: Patient visits increased from 5,664 in 2020 to 11,851 in 2024, while cancer-related hospitalizations rose from 1,477 to 6,102. The average waiting time for reception was reduced from 12 to 7 hours, and the processing time for documentation was reduced from 45 to 15 minutes. The introduction of digital solutions improved the accuracy of admission and reduced the number of inappropriate hospitalizations. Improvements in identifying clinical contraindications and infectious risks through remote screening technologies were also noted. The number of telemedicine consultations increased 3 times, especially in surgery and transplantology.

Conclusion: Digital transformation has significantly improved admissions efficiency, improving patient flow, reducing processing time and improving decision-making. Further development of digital infrastructure and staff competencies is recommended to ensure sustainable growth and quality of care in cancer care. The comprehensive implementation of telemedicine and interaction with air ambulance contribute to increasing the availability of cancer care, optimizing resources and reducing costs.

Keywords: Hospitalization; Oncology; Health Information Systems; Workflow Optimization; Digital Health; Patient Flow; Telemedicine

Introduction

Introduction Ensuring timely and effective oncological care is a priority task of the health care system of the Republic of Kazakhstan. Cancer continues to occupy a leading position among the causes of morbidity and mortality, putting increasing pressure on the national health care system. In this regard, early diagnosis and optimization of hospitalization processes play a key role in improving survival and improving the quality of life of patients with cancer.

Admission departments act as the first line of inpatient care and are the primary point of contact of patients with the medical system. Their main functions include triage, registration, identification, routing and documentation - all of these processes directly impact hospital capacity, patient safety and staff workload. In oncological institutions, the timeliness of admission is especially important: delays can lead to missed treatment options and a worsening of the prognosis. Therefore, improving the efficiency of admission departments is a prerequisite for high-quality cancer care.

In recent years, Kazakhstan has been actively pursuing reforms in healthcare aimed at digital transformation and increased transparency. Programs such as the Unified National Health System, the implementation of the Electronic Health Record (EMC) and the Electronic Inpatient Registry (ERSB) have dramatically changed the way health information is collected, processed and shared [1]. Digitalization in healthcare is seen not only as a technological solution, but also as an instrument of public policy.

The Ministry of Health of the Republic of Kazakhstan has consolidated its expectations from medical institutions in a number of official regulatory documents. In particular, Order No. IP DSM-225/2020 regulates the structure and functioning of admission departments, establishing requirements for infrastructure, document management and patient routing [2]. In addition, Order No. RK DSM-27 (2022) defines the procedure for the provision of medical care to patients with cancer, including hospitalization criteria, pre-selection and interdisciplinary interaction [3].

These regulations are based on the Code of Public Health and the Health Care System of the Republic of Kazakhstan No. 360-VI (2020), which emphasizes the principles of a patient-oriented approach, digital integration and continuous quality improvement [4].

Limited Liability Partnership "National Research Oncological Center" (NROC), located in Astana, is one of the leading oncological institutions in Kazakhstan. In addition to clinical activities, it serves as a research and innovation center. Over the past five years, the NROC has implemented a number of projects to digitalize patient admission processes, including electronic triage, remote verification of diagnoses and integration with national digital platforms.

In the context of digitalization of all spheres of life, healthcare is actively introducing innovative approaches to the provision of medical care. One of these areas is telemedicine - a system for the provision and receipt of medical services using remote technologies. According to the definition of the World Health Organization (WHO), telemedicine contributes to improving the availability of medical care, reducing the burden on hospitals and improving the quality of treatment through prompt communication between medical specialists. According to WHO, telemedicine technologies began to be introduced in Kazakhstan since 2004 [5].

NROC began using telemedicine in 2015. Today, along with traditional face-to-face care, the center actively uses digital tools in diagnosis, monitoring and treatment, especially in the areas of transplantation and oncology. Modern technologies allow doctors to consult patients after liver and kidney transplants, providing control over their condition, regardless of the region of residence.

Particular attention is also paid to emergency situations. If the telemedicine consultation indicates the need for face-to-face intervention, and the patient is not transportable, the specialists of NROC leave with the help of air ambulance and provide assistance on the spot. Thus, telemedicine becomes a link between highly specialized medicine and the needs of the regions.

In terms of legal regulation, telemedicine practice in Kazakhstan is based on the provisions of the Law of the Republic of Kazakhstan "On People's Health and the Health Care System" (as amended in 2020), as well as a number of by-laws. The country has approved standards for the provision of remote medical services and established procedures for maintaining electronic medical records, which together form a regulatory framework for the integration of digital technologies into the healthcare system [6].

Given the growing workload, the complexity of cancer care and the course towards digital transformation of healthcare, an analysis of the effectiveness of the NROC admission department is especially relevant. This study is aimed at studying the evolution of admission processes, assessing the results achieved and compliance with the requirements of the Ministry of Health of the Republic of Kazakhstan, as well as identifying factors contributing to sustainable development.

Materials and Methods

The study used a retrospective mixed method covering the period from January 2020 to December 2024. Within the framework of the methodology, a quantitative analysis of the performance indicators of the NROC admission department was carried out, as well as a qualitative assessment of its compliance with the current regulatory documents in the field of health.

Data sources

Data were collected from internal NROC information systems, including:

- Electronic patient logs,
- Hospitalization registers,
- Annual reports on the activities of the subdivision,
- Patient routing systems,
- Integrations with the Electronic Inpatient Registry (ERSB) and the National Health Platform.

Patients were classified by year of presentation, nosological form, source of referral (outpatient clinic, emergency, screening), and reason for hospitalization. Personal data were depersonalized in accordance with the Law of the Republic of Kazakhstan "On Personal Data and Their Protection" [6].

Key Performance Indicators (KPIs)

The assessment included the following indicators:

- Total number of requests,
- Hospitalizations for oncological diagnoses,
- Average reception time (from arrival to accommodation),
- Medical record time,
- Proportion of failures in hospitalization,
- The level of digitalization was assessed using a 0–5 scoring system, where each core component (electronic triage, remote pre-registration, automated verification modules, integration with national health platforms, interoperability with external diagnostics) contributed 1 point. A total score of 0 indicated no digitalization, while 5 indicated full implementation of all modules.

These indicators comply with international recommendations (for example, WHO) and the requirements of the Ministry of Health of the Republic of Kazakhstan, fixed in orders No. IP-DSM-225/2020 and No. IP-DSM-27/2022 [2,3,5].

Regulatory Review

NROC practice was compared with the current legislation on the basis of the following documents:

- Order No. IP-DSM-225/2020 - defines the standards for the operation of reception offices [2],
- Order No. IP-DSM-27/2022 - On approval of the Standard for the organization of medical care in inpatient conditions in the Republic of Kazakhstan [3],
- Order No. IP-DSM-27/2022 - On approval of the Standard for the Organization of Emergency Medical Care in the Admission Departments of Medical Organizations Providing Medical Care in Inpatient Conditions in the Republic of Kazakhstan [7].
- Code of the Republic of Kazakhstan No. 360-VI - general legislation in the field of health care [4].

An expert assessment of the compliance of all stages of patient admission with the current standards was carried out.

An important direction in the development of telemedicine at NROC was its combination with the work of air ambulance. In cases where remote interaction with the patient is not enough, specialists fly out to conduct face-to-face consultations, perform surgical interventions on the spot, or transport severe patients to the NROC.

Within the framework of the article, a descriptive statistical analysis was conducted on telemedicine consultations carried out by NROC during the period from 2020 to 2024. A total of 1,120 consultations were recorded over this time. The information was systematized by year, specialist profiles, and regions from which the requests originated. The data are presented in summary tables and analyzed to identify trends and priority areas.

Digitalization assessment

The study analyzed the degree of implementation of digital solutions:

- Software (SmartHosp, EPB),
- Module implementation dates,
- Use of digital verification and pre-registration,
- Interviews with medical and IT specialists of the NROC.

Performance indicators (time, errors, staff satisfaction) and the degree of integration with public health systems were highlighted.

The effective deployment of telemedicine depends on a robust and integrated technological infrastructure encompassing both hardware and software components. At the National Research Oncology Center, as well as in other medical organizations across Kazakhstan, a range of advanced technical solutions has been implemented to ensure reliable and secure remote care delivery.

Key components include:

Telemedicine complexes – mobile diagnostic and consultation stations capable of transmitting high-quality video and medical data in real time, enabling timely specialist input regardless of patient location.

Video conferencing systems – platforms such as Zoom for Healthcare, Cisco Webex, and domestic

analogues, integrated with secure communication channels to ensure confidentiality and compliance with national data protection standards.

Medical diagnostic equipment with remote data transfer – including portable ultrasound devices, electrocardiographs (ECG), and endoscopic systems, enabling immediate sharing of results with consulting physicians.

Specialized software solutions – integration with the Unified Medical Information and Analytical System (UMIAS RK), Hospital Information System (HIS), and Picture Archiving and Communication Systems (PACS) to streamline patient data access, imaging management, and multidisciplinary collaboration.

Looking ahead, promising directions for technological advancement include the integration of artificial intelligence (AI) tools for automated interpretation of medical images, predictive analytics, and the generation of personalized clinical recommendations. Additionally, the use of wearable medical devices—such as smart bracelets and continuous monitoring sensors—offers opportunities for ongoing remote health surveillance, enabling early detection of changes in patient condition and reducing the need for in-person visits.

Results

In the period from 2020 to 2024, the admission department of the NROC demonstrated a significant increase in the volume of work and an improvement in efficiency indicators. This section presents the quantitative and qualitative results of the study.

Table-1. Increase in complaints and hospitalizations

Year	Total Patient Visits	Oncology-specific Hospitalizations	Hospitalization Refusals	Avg. Admission Time (hrs)	Avg. Document Processing Time (min)
2020	5,664	1,477	119 (2.1%)	12	45
2021	7,402	2,835	102 (1.4%)	10	35
2022	9,018	4,200	83 (1.1%)	9	25
2023	10,987	5,301	71 (0.9%)	8	20
2024	11,851	6,102	55 (0.5%)	7	15

The total number of requests has more than doubled. The number of hospitalizations of cancer patients has quadrupled, which indicates both an increase in cancer incidence and the effectiveness of referrals. Hospital refusals decreased by more than 75%, indicating improved triage and accuracy of patient pre-assessment.

Reduced time for reception and documentation

An important area of the center's work was the introduction of digital pre-registration, identification of patients through barcodes and electronic certificates, integration with external diagnostic institutions, SmartHosp and ESD modules, which made it possible to significantly optimize the hospitalization processes. The use of patient routing algorithms and automated data recording helped to reduce the average waiting time for hospitalization from 12 to 7 hours, and the duration of medical documentation decreased by 66.7% - from 15 to 45 minutes. These changes have improved the efficiency of the admission department, as well as reducing the burden on patients and medical personnel.

As part of improving the organization of work and digitalization of processes in a medical institution, a phased modernization plan was implemented. In 2020-2021, electronic forms of patient sorting and a system of electronic registration and sorting units (ERSB) were introduced, which made it possible to speed up data processing and increase the accuracy of flow distribution.

In 2022, full integration with the National Health Platform was completed, ensuring uninterrupted exchange of health information between institutions and government systems.

According to internal surveys conducted after the introduction of digital solutions, significant positive changes were achieved. The administrative burden on staff was reduced by 30%, which allowed employees to devote more time to direct medical care. The level of employee satisfaction has increased significantly due to the simplification of work processes and a decrease in routine operations. In addition, the number of errors in the preparation of documentation decreased from 4% to less than 1%, which had a positive effect on the quality

and accuracy of medical records.Regulatory Compliance Assessment

The activities of the admission department were compared with the requirements:

- Order No. IP-DSM-225/2020 (structure, flows, premises, documentation); [2]
- Order No. IP-DSM-27/2022 (procedure for providing oncological care, hospitalization criteria). [7]

Legal regulation and ethical aspects of telemedicine

In Kazakhstan, the legal basis for the provision of medical care using telemedicine is enshrined in Order of the Ministry of Health of the Republic of Kazakhstan dated February 1, 2021 No. IP DSM-12/2021, which determines the procedure for remote consultations, a list of permissible services and requirements for technical equipment [8].

Since 2023, amendments have been made to strengthen the requirements for:

- protection of personal data of patients (according to the Law of the Republic of Kazakhstan "On Personal Data and Their Protection");
- use of secure communication channels;
- mandatory informed consent to remote consultation;
- storage of medical records in electronic form during the period established by law.

The key ethical aspect remains ensuring the confidentiality and security of data, preventing unauthorized access, as well as respecting the rights of patients to refuse telemedicine in favor of face-to-face admission.

In international practice, the regulation of telemedicine is based on standards such as the General Data Protection Regulation (GDPR) in the European Union and the Health Insurance Portability and Accountability Act (HIPAA) in the United States. These regulatory frameworks can serve as a reference point for the further development of telemedicine legislation in the Republic of Kazakhstan [9].

Table- 2. Dynamics of telemedicine consultations by years

Year	Number of consultations
2020	35
2021	109
2022	309
2023	303
2024	364

In 2020, despite the outbreak of the COVID-19 pandemic, the number of telemedicine consultations remained minimal (35), likely due to logistical constraints, a heavy burden on the healthcare system, and the urgent need to restructure processes [10]. Since 2021, there has been a steady increase in the number of online consultations, which may indicate NROC's adaptation to new conditions and the gradual implementation of telemedicine solutions.

Expert Advice Analysis

The largest number of consultations was recorded in the following areas:

- Nephrologist - 389 consultations (high activity is explained by the need for long-term follow-up of patients after kidney transplantation).
- Hematologist - 198 consultations (including oncohematology).
- Hepatologist - 176 consultations (related to liver transplantation and chronic hepatitis).
- Vascular surgeon - 111 consultations.
- Surgeons (abdominal and thoracic) - 87 consultations.

Table- 3. Dynamics of telemedicine consultations

Field	2020	2021	2022	2023	2024
Surgeon	7	23	29	6	22
Vascular Surgeon	2	1	46	27	35
Urologist		2	3	1	3
Transplantologist		3	4	6	7
Oncologist		1	5	5	6
Traumatologist		1	3		6
Chemotherapist			2	2	12
Nephrologist		31	120	140	98
Hepatologist	11	29	30	44	62

Hematologist	6	14	34	60	84
Otorhinolaryngologist		1	2		
Resuscitator	4	7	17	8	15
Cardiologist		2	5		
Reconstructive Surgeon				1	
Neurologist				1	
Gynecologist				1	
Radiation Therapist					4
Oncology Surgeon Of The Head And Neck Sector					4
Others		2	9	1	6

Consultation analysis by region

The greatest activity was noted from the following regions:

- Mangystau region - 103 consultations
- West Kazakhstan region - 95
- Kostanay region - 67
- Zhambyl region - 63
- Shymkent - 70
- Aktobe region - 59
- Atyrau region - 58

This picture indicates a high level of need for oncological and transplantation care in these regions. It is noteworthy that Almaty and Astana, despite the presence of a developed medical and technical base, also actively interact with NROC through telemedicine channels, which indicates the demand for expert support even in large cities.

Table- 4. Dynamics of telemedicine consultations by region

	2020	2021	2022	2023	2024
Akmola region		9	30	26	17
Mangystau region		13	29	22	39
Atyrau region		15	23	21	19
Kyzylorda region		4	15	23	12
Turkestan region			3	18	21
Karaganda region		4	6	7	16
North Kazakhstan region		4	17	10	5
East Kazakhstan region		4	7	9	10
Pavlodar region		5	8	12	9
Aktobe region		8	18	18	15
Kostanay region		12	5	14	36
Abay region			6	12	5
Zhambyl region		4	8	18	33
Shymkent		12	18	10	30
West Kazakhstan region		10	11	38	36
Astana			4	12	15
Zhetysu region			10	5	15
Ulytau region		5	10	4	7
Almaty				24	18

Telemedicine consultations and air ambulance

In the period 2020-2024 28 such flights were performed, the structure of which is shown in Table 5. Structure and Dynamics of Air Ambulance Missions (2020–2024).

Table- 5. Structure and Dynamics of Air Ambulance Missions (2020–2024)

Year	Number Of Departures	On-Site Operations	Personal Consultations	Patient Transport
2020	6	5	–	1
2021	5	2	–	1
2022	3	3	–	–
2023	5	4	2	–
2024	9	9	–	–

The dynamics show an increase in activity in 2024, when the number of air ambulance departures increased 1.8 times compared to the previous year, while all departures were accompanied by surgical interventions on the spot. This indicates an increase in the level of equipment of field teams and the effectiveness of integrating telemedicine technologies with emergency medical care.

As a result of an audit of the Ministry of Health conducted at the end of 2023, the department demonstrated more than 95% compliance with the standards.

Discussion

This retrospective, single-center study conducted at the National Research Oncology Center (NROC) between 2020 and 2024 provides valuable insights into the evolving role of digital technologies and telemedicine in optimizing hospital admission processes and expanding access to specialized care. While the descriptive nature of the data limits the ability to draw causal conclusions, the observed trends suggest meaningful improvements in operational efficiency, clinical coordination, and regulatory alignment.

Growth in Patient Volume and Efficiency Indicators

Over the five-year period, the admission department experienced a substantial increase in workload, with the total number of patient visits more than doubling. Oncology-specific hospitalizations rose from 1,477 in 2020 to 6,102 in 2024, indicating both a growing demand for oncological services and potentially improved referral mechanisms. The reduction in hospitalization refusals—from 2.1% to 0.5%—may reflect enhanced triage protocols, better pre-admission assessments, and more accurate patient routing.

These quantitative shifts were accompanied by notable improvements in time-related metrics. The average admission time decreased from 12 to 7 hours, while documentation processing time dropped by 66.7%, from 45 to 15 minutes. These changes coincided with the implementation of digital pre-registration systems, barcode-based patient identification, and integration with external diagnostic platforms such as SmartHosp and ESD modules. The introduction of patient routing algorithms and automated data entry tools likely contributed to these gains by reducing administrative redundancy and streamlining workflows.

Internal surveys conducted post-implementation revealed a 30% reduction in administrative burden on staff, allowing clinicians to allocate more time to direct patient care. Additionally, the error rate in medical documentation preparation decreased from 4% to less than 1%, suggesting improved data accuracy and record quality. Staff satisfaction also increased, attributed to the simplification of routine tasks and the overall modernization of work processes.

Expansion and Impact of Telemedicine

Telemedicine emerged as a critical component of NROC's digital transformation strategy. The number of remote consultations grew from just 35 in 2020 to 364 in 2024, reflecting a tenfold increase. This upward trend began in 2021, likely driven by the need to adapt to pandemic-related constraints and the broader push toward digital healthcare solutions. The data suggest that telemedicine became an increasingly accepted and integrated modality for delivering care, particularly in specialties requiring long-term follow-up and interdisciplinary collaboration.

Nephrology accounted for the highest number of consultations (389), followed by hematology (198) and hepatology (176). These specialties are closely linked to transplant medicine and chronic disease management, where continuous monitoring and timely expert input are essential. Other areas such as vascular surgery, abdominal and thoracic surgery, and resuscitation also demonstrated consistent engagement, albeit at lower volumes.

While some fields—such as oncosurgery of the head and neck, chemotherapy, and otorhinolaryngology—showed limited telemedicine

activity, their inclusion underscores the model's relevance even in complex clinical scenarios. In many cases, telemedicine served as a preliminary step, followed by in-person visits, mobile team deployment, or hospitalization. This hybrid approach highlights the flexibility and adaptability of remote care models in supporting decision-making and ensuring continuity of care.

Regional Distribution and Equity of Access

Analysis of consultation data by region revealed significant engagement from areas such as Mangystau, West Kazakhstan, and Kostanay, suggesting a high demand for specialized services in regions with limited local capacity. Interestingly, major urban centers like Almaty and Astana also actively utilized telemedicine channels, indicating that expert support remains valuable even in well-equipped settings. This pattern points to telemedicine's potential to bridge geographic disparities and enhance equity in healthcare access across Kazakhstan [12].

Integration with Air Ambulance Services

A notable innovation was the integration of telemedicine with air ambulance operations. Between 2020 and 2024, NROC conducted 28 field missions, with a marked increase in 2024. That year, all nine departures included on-site surgical interventions, reflecting improved equipment, team readiness, and coordination. This synergy between remote consultations and emergency response capabilities enabled timely care delivery in remote areas and reduced delays in critical interventions.

Regulatory Alignment and Ethical Considerations

The transformation of the admission department was guided by national regulatory frameworks, including Order No. IP-DSM-225/2020 and Order No. IP-DSM-27/2022 [2,3]. These directives provided clear guidelines for structuring workflows, defining patient routes, and standardizing documentation. A Ministry of Health audit conducted in late 2023 confirmed over 95% compliance with these standards, underscoring the department's commitment to regulatory adherence.

Telemedicine practices were governed by Order No. IP DSM-12/2021, which outlined the scope of permissible services, technical requirements, and consultation procedures [8]. Amendments introduced in 2023 strengthened provisions related to data protection, secure communication, informed consent, and electronic record storage. Ethical considerations—particularly around confidentiality, patient autonomy, and the right to opt for in-person care—remain central to telemedicine implementation.

Internationally, frameworks such as the General Data Protection Regulation (GDPR) in the European Union and the Health Insurance Portability and Accountability Act (HIPAA) in the United States offer valuable models for further refinement of Kazakhstan's telemedicine legislation. These standards emphasize patient rights, data security, and accountability, which are essential for building trust and ensuring sustainable adoption [11].

Limitations

It is important to acknowledge the limitations of this study. As a retrospective, single-center analysis, the findings are inherently descriptive and cannot establish causality or be generalized to the broader healthcare system. The data reflect the specific context of NROC and may not capture variations in implementation, infrastructure, or patient demographics across other institutions. Future research should include multi-center, prospective studies with control groups to validate these observations and assess long-term clinical and economic outcomes.

Challenges

Despite these advances, the implementation process revealed several operational and organizational challenges. Staff resistance, especially during the initial phases of IT system implementation, highlighted the pivotal role of human factors in the success of digital transformation. This resistance was primarily driven by limited familiarity with new technologies, apprehension about potential changes in workload, and the challenges associated with adjusting to updated operational procedures. Additionally, occasional digital infrastructure failures highlighted the importance of robust technical readiness and system redundancy to prevent disruptions in patient care.

A further obstacle was the shortage of specialists proficient in managing and maintaining digital medical systems, which slowed the pace of adoption and placed added strain on existing IT teams. These challenges underline the necessity of comprehensive pre-implementation planning, ongoing technical support, and a phased, iterative approach to introducing innovations—allowing gradual adaptation and minimizing operational risks.

Recommendations and Lessons Learned

Drawing on this experience, the NROC's journey offers a set of actionable recommendations for other healthcare institutions in Kazakhstan and the wider Central Asian region:

1. Conduct a regulatory audit before launching digital initiatives to identify

alignment gaps, ensure compliance, and streamline approval processes.
2. Integrate KPI monitoring systems into routine workflows to enable data-driven decision-making and maintain accountability at all operational levels.
3. Establish continuous collaboration with government agencies to ensure adherence to evolving legislation, secure stable funding, and coordinate large-scale implementation efforts.

Ultimately, the integration of digitalization with a well-structured regulatory framework produces benefits that extend beyond technical modernization. It fosters strategic improvements in service delivery, enhances institutional resilience, and supports the long-term sustainability of the healthcare system. The NROC's case demonstrates that when innovation is anchored in clear, adaptable regulations, it can yield transformative outcomes—serving as a model for other specialized institutions in Kazakhstan and beyond.

Conclusion

This study provides a comprehensive evaluation of the admission department's performance at the National Research Oncology Center from 2020 to 2024, highlighting the transformative role of digitalization and regulatory alignment in oncology care. Strategic integration of pre-registration, digital triage, and interoperability with national systems (EPSS, EMC, SmartHosp), in compliance with Ministry of Health standards, has led to measurable improvements, including more than a twofold increase in patient flow, a fourfold rise in oncological hospitalizations, and a >75% reduction in hospitalization refusals.

The data suggest that telemedicine in Kazakhstan already serves as an effective tool in highly specialized fields such as oncology and transplantology, contributing to improved access to specialized care, optimized patient routing, reduced inpatient burden, and enhanced cost-effectiveness. Sustained progress will require continued legal framework development, workforce training, technical infrastructure enhancement, and integration with AI-driven analytics.

NROC's experience demonstrates that the combination of advanced information technologies and supportive regulatory policy enables the creation of an effective, safe, and sustainable model for oncology care delivery. This model has the potential to be adapted in other specialized institutions across Kazakhstan and Central Asia; however, its replicability and applicability at the systemic level require validation through comparative or multicenter studies.

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Review Article

The Role of Liquid Biopsies in Tracking Tumor Evolution and Overcoming Therapeutic Resistance in Cancer

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Abstract:
Liquid biopsies have developed as a revolutionary technique in cancer diagnosis, treatment evaluation, and the detection of therapeutic resistance. Unlike traditional tissue biopsies, which are invasive and limited to a single temporal analysis, liquid biopsies offer a non-invasive, real-time evaluation of tumour dynamics through the analysis of biomarkers such as circulating tumour DNA (ctDNA), circulating tumour cells (CTCs), exosomes, and microRNAs. This approach enables continuous monitoring of tumour advancement, allowing for the early detection of cancer, the tracking of minimal residual disease, and the identification of emerging resistance mutations. As cancers advance and acquire resistance to therapies, liquid biopsy provides critical information that enables clinicians to customise treatment strategies and improve outcomes. Despite challenges such as sensitivity limitations in early-stage cancers and the necessity for standardised testing protocols, technological advancements, including next-generation sequencing (NGS), CRISPR, and AI-driven analytics, are enhancing the precision and accessibility of liquid biopsies. Through ongoing validation and cost-reduction efforts, liquid biopsies are set to become essential to precision oncology, offering a transformative approach to cancer therapy that could improve patient outcomes and foster equitable healthcare globally.

Keywords: Liquid Biopsy; Circulating Tumor DNA (ctDNA); Therapeutic Resistance; Minimal Residual Disease (MRD); Precision Oncology

Introduction

Overview of Liquid Biopsy

Non-invasive liquid biopsy examines blood, urine, or saliva to identify and track malignancy. Liquid biopsies offer real-time genetic profiling of tumours without the need for invasive surgery. This approach focusses on biomarkers such as ctDNA, CTCs, exosomes, and microRNAs derived from bodily fluids. Liquid biopsy can identify mutations, track disease progression, and inform customised treatment without the need for repeated invasive procedures, rendering it highly favoured in oncology [1].

Relevance to Tumor Evolution and Therapeutic Resistance

Cancer cells undergo genetic and epigenetic evolution to promote disease progression, metastasis, and resistance to therapy. These modifications can transpire rapidly, leading to resistant subclones that obstruct chemotherapy, targeted therapies, and immunotherapy. Liquid biopsy facilitates the monitoring of tumour evolution and the understanding of genetic alterations and clonal dynamics that contribute to therapeutic resistance. Liquid biopsy enables clinicians to monitor disease development and identify resistance mutations in real time, facilitating adjustments to treatment programs. Enhanced patient outcomes rely on non-invasive tumour monitoring [2].

Objective of the Review

Liquid biopsies may facilitate the monitoring of tumour growth and address resistance to cancer therapies. This review will examine ctDNA, CTCs, and exosome liquid biopsies, along with their clinical applications in mutation identification, therapy response assessment, and therapeutic decision-making. The review will examine the existing limitations of liquid biopsy technologies and potential advancements that may enhance their therapeutic efficacy. This thorough review investigates the impact of liquid biopsies on oncology and the provision of novel tailored cancer treatment alternatives.

Background

Traditional Biopsy Limitations

Although crucial for cancer diagnosis and monitoring, traditional tissue biopsy possesses considerable limitations. The primary disadvantage of surgery to excise tissue samples is the potential threat it poses to patients, particularly those with advanced or metastatic cancers. Tissue biopsies are typically performed singularly, complicating the monitoring of tumour activity such as mutations or clonal evolution throughout treatment. Tumours exhibit heterogeneity, as distinct subclones possess varying molecular characteristics; therefore, a single biopsy may not comprehensively represent the genetic diversity. This limitation may hinder the identification of resistant mutations or the advancement of cancer in reaction to treatment [3].

Introduction of Liquid Biopsies

Liquid biopsies serve as a non-invasive alternative to tissue biopsies, mitigating the associated downsides. Liquid biopsies, introduced in the early 2000s, diagnose and monitor cancer through the use of biomarkers such as ctDNA, CTCs, and exosomes in blood samples. Liquid biopsies are simple to obtain, may be performed often without causing patient discomfort, and may provide superior insights into tumour dynamics. Advancements in next-generation sequencing (NGS) and microfluidics enhance the precision of liquid biopsy procedures, rendering them effective for early cancer detection, monitoring, and tracking therapy resistance [4].

Tumor Heterogeneity and Resistance

Cancer is complex and heterogeneous, exhibiting diverse genetic and epigenetic patterns across distinct tumour regions or metastases. Clonal evolution generates subclones exhibiting varying treatment sensitivities or resistances as a result of mutations. As cancers progress, they frequently acquire resistance to therapies, rendering previously effective treatments ineffective. Cancer's dynamic nature necessitates continuous surveillance for mutations and clonal alterations. Liquid biopsies provide the real-time identification of cancer evolution and resistance mutations by capturing genetic material shed from tumours into the circulation, thereby informing treatment decisions and enhancing patient outcomes [5].

Types of Liquid Biopsies

Circulating Tumor DNA (ctDNA)

Liquid biopsy depends on circulating tumour DNA (ctDNA), which consists of fragmented DNA released by cancer cells into the bloodstream. ctDNA analysis can identify mutations, genetic alterations, and resistance mutations in tumours without the need for tissue biopsies. The primary function of ctDNA in liquid biopsy is to represent the tumor's genetic composition and monitor cancer growth. ctDNA can contemporaneously monitor cancer genetic mutations in response to treatments, elucidating therapeutic efficacy and resistance mechanisms.

One of the primary advantages of ctDNA is its exceptional sensitivity in identifying minimal residual disease (MRD), the minute quantity of cancer cells that persist post-therapy and have the potential to return. Circulating tumour DNA (ctDNA) is crucial for early-stage cancer screening and post-treatment surveillance, as it can be identified even with a modest tumour burden. ctDNA analysis can identify residual disease prior to clinical signs of relapse, facilitating early intervention and tailored treatment [6].

In certain cancers or patients with modest tumour burden, the sensitivity of ctDNA may be compromised by inadequate circulation. The kind of tumour and the ctDNA extraction technique can influence the identification of certain mutations, highlighting the necessity for standardisation and enhancement.

Circulating Tumour Cells (CTCs)

Circulating tumour cells (CTCs) are individual cancer cells or small clusters that have detached from the primary tumour or metastases and have entered the bloodstream. Circulating tumour cells (CTCs), a promising liquid biopsy biomarker, indicate cancer dissemination, progression, and therapeutic resistance. Through the extraction and analysis of circulating tumour cells (CTCs), physicians can identify cancer dissemination, metastatic disease, and genomic characteristics of CTCs to inform personalised treatment strategies [7].

Circulating tumour cells (CTCs) can identify therapeutic resistance by revealing real-time genetic and phenotypic changes in the cancer. When a medicine reduces tumour size but CTC analysis reveals resistance mutations, physicians may modify the treatment. Real-time resistance monitoring decreases treatment delays and enhances outcomes [8].

Circulating CTCs are few, complicating investigation. Circulating tumour cells (CTCs) are infrequent, particularly in early-stage malignancies characterised by confined illness, hence complicating their detection and separation. Microfluidics and immunomagnetic capture technologies enhance circulating tumour cell (CTC) isolation; however, obtaining high-quality CTCs for subsequent molecular analysis remains challenging [9].

Exosomes and MicroRNAs

Exosomes transport proteins, lipids, and nucleic acids from the tumour to the bloodstream. These vesicles communicate between cells and promote tumour growth, metastasis, and therapy resistance. Exosomes carry tumor-specific mutations and non-coding RNAs, making them useful liquid biopsy biomarkers. Cancer liquid biopsies have focused on exosomal miRNAs as biomarkers [10].

Cancer commonly alters miRNAs, tiny non-coding RNAs that influence gene expression. Exosomal miRNAs reveal tumour features, progression, and treatment resistance pathways. MiRNAs are persistent in body fluids and less prone to degradation, making exosome identification a dependable and non-invasive technique to monitor cancer dynamics.

Exosomes and miRNAs are still being tested as liquid biopsy indicators. Isolating exosomes from complicated bodily fluids and standardising their characterisation techniques are difficult. Exosome-based liquid biopsies may be useful for real-time cancer monitoring, but additional study is needed to validate and standardise methods [11].

Other Emerging Biomarkers

Besides ctDNA, CTCs, and exosomes, various indicators are being studied for liquid biopsy. Long non-coding RNAs (lncRNAs) regulate gene expression and are linked to cancer start and progression. LncRNAs are persistent in plasma and serum and may reveal tumour behaviour and therapy response [12].

Proteins and metabolites are promising liquid biopsy candidates. Tumor-derived proteins like CA-125 and EGFR can be found in the circulation and indicate tumour progression and therapy resistance. Circulating metabolites also reflect tumour metabolism, giving a non-genetic way to track tumour dynamics [13].

These developing biomarkers offer new liquid biopsy potential, but detection sensitivity, specificity, and clinical validation remain problems. As the science improves, multi-omics techniques with many biomarker types may improve liquid biopsies for cancer diagnosis and therapy monitoring.

Liquid biopsy methods based on ctDNA, CTCs, exosomes, and developing biomarkers have great potential for real-time cancer surveillance and personalised treatment. Each form of biomarker has its own limitations, but improved detection technologies and clinical relevance will certainly increase their use in oncology. Liquid biopsy is becoming a popular non-invasive cancer diagnostic, monitoring, and treatment tool. Fig 1 shows how liquid biopsy indicators such cfDNA, ctDNA, and CTCs monitor tumour state from diagnosis to treatment and recurrence [14].

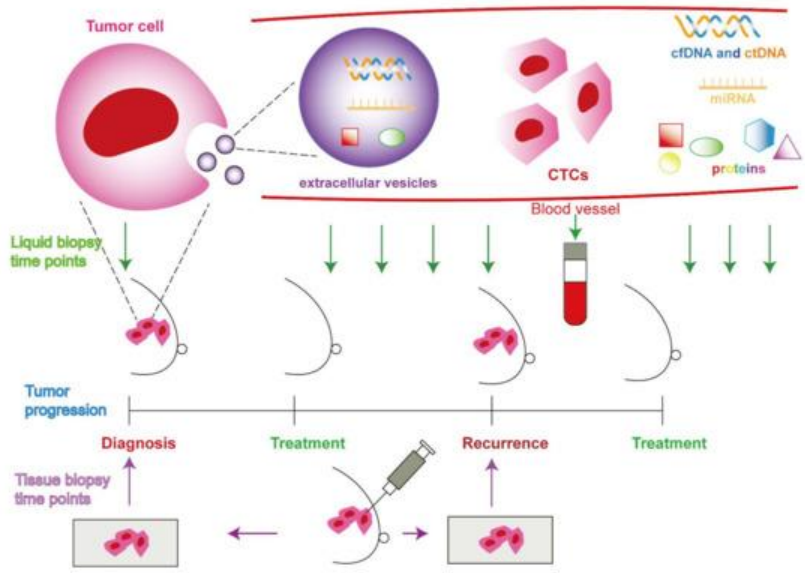

Fig 1 Liquid Biopsy and Tumor Progression Monitoring: A Visual Guide. This figure illustrates the key components involved in liquid biopsy for cancer monitoring, including tumor cells, extracellular vesicles, and circulating tumor cells (CTCs). The image highlights the use of cfDNA, ctDNA, miRNA, and proteins as biomarkers for tumor progression at various time points, such as diagnosis, treatment, and recurrence. The diagram also contrasts liquid biopsy with tissue biopsy, emphasizing its relevance at different stages of cancer management.Zhu, X., Wu, J., Xu, J., et al. (2020).

Mechanisms of Tumor Evolution and Therapeutic Resistance

Genetic Mutations and Clonal Evolution

Genetic mutations facilitate the evolution of cancer throughout time. Genetic alterations in cancer cells override normal cellular regulations, resulting in unchecked proliferation and spread. Errors in DNA replication and exposure to carcinogens induce genetic mutations. As cancer progresses, genetic heterogeneity increases, resulting in a diverse population of tumour cells, referred to as "clonal evolution." Mutations in tumour subclones can enhance proliferation, facilitate immune evasion, and confer treatment resistance [15].

Liquid biopsy is an effective technique for the real-time detection of genetic abnormalities. Liquid biopsy analyses circulating tumour DNA (ctDNA) from bodily fluids, providing insights into the tumor's genetic landscape and facilitating the identification of mutations, deletions, and amplifications linked to tumour evolution. As malignancies progress, specific mutations or genetic anomalies may become more pronounced, fostering resistance to therapies. In non-small cell lung cancer (NSCLC), mutations in the EGFR gene, such as exon 19 deletions or T790M, may develop over time, resulting in resistance to first-line EGFR treatments. Liquid biopsy facilitates the ongoing surveillance of these mutations, allowing for prompt intervention and modifications in treatment [16].

Tumor Microenvironment

The advancement of cancer and resistance to therapy are influenced by the tumour microenvironment (TME). The tumour microenvironment comprises non-malignant cells such as fibroblasts, immune cells, blood vessels, and extracellular matrix constituents that influence tumour cells. Modifying the TME can induce significant changes that promote resistance. Cancer-associated fibroblasts (CAFs) can shield cancer cells from chemotherapy-induced apoptosis, whereas tumor-infiltrating immune cells can enhance or inhibit tumour immunity.

Cell-free DNA (cfDNA) and RNA from the tumour microenvironment (TME) can be obtained using liquid biopsy, elucidating the influence of the TME on resistance mechanisms. Both cancerous and non-tumor cells release cfDNA, which can signify abnormalities in the tumour microenvironment, such as hypoxia, angiogenesis, and immunological modulation. Exosomal RNA from the cancer and adjacent stromal cells provide essential insights on the tumor's therapeutic response and developing resistance mechanisms. Through liquid biopsy, clinicians can identify genetic modifications in the tumour as well as the dynamic interactions between the tumour and its environment that lead to therapeutic resistance [17,18].

Therapeutic Resistance Mechanisms

Tumours often acquire resistance to chemotherapy, immunotherapy, and targeted medicines, making cancer treatment difficult. Mutations, TME changes, and compensatory signalling

pathways drive these resistance mechanisms. One prevalent [19] cause of chemotherapy resistance is the selection of tumour cells with mutations in genes involved in drug metabolism, efflux, or DNA repair. Mutations in the TP53 gene, which encodes the tumour suppressor p53, often cause cisplatin resistance in many malignancies [19]. Mutations can be detected by liquid biopsy, identifying people at risk for poor treatment outcomes.

- Immunotherapy Resistance: While immunocheckpoint inhibitors (ICIs) like pembrolizumab and nivolumab have revolutionised cancer treatment, not all patients respond. Mutations in genes like PD-L1 or tumour antigen presentation abnormalities can cause immunotherapy resistance. Liquid biopsy can predict immunotherapy response by detecting immune-related gene changes such PD-L1 expression or tumour antigen-presenting machinery mutations [20].
- Targeted Therapy Secondary mutations that bypass the blocked route cause targeted therapy resistance. The T790M mutation in the EGFR gene hinders first-generation EGFR inhibitors from attaching to NSCLC cells, causing resistance. Similar to colorectal cancer, KRAS mutations can cause EGFR-targeted therapy resistance. Liquid biopsy can detect ctDNA resistance mutations in real time, guiding therapeutic changes and detecting resistant clones.

Genetic mutations, TME alterations, and adaptive signalling pathways constitute the complicated mechanisms of cancer treatment resistance. Liquid biopsy can identify these changes, enabling tumour evolution tracking and personalised treatment adjustments. Liquid biopsy helps overcome therapeutic resistance and improve clinical outcomes by detecting genetic alterations, immune-related indicators, and extracellular variables [21].

Fig 2 shows the intricate interactions that affect tumour immune evasion and cancer therapy efficacy. It classifies these components as tumor-intrinsic, tumour microenvironmental, and host-related, each contributing to cancer therapy's dynamic immune response.

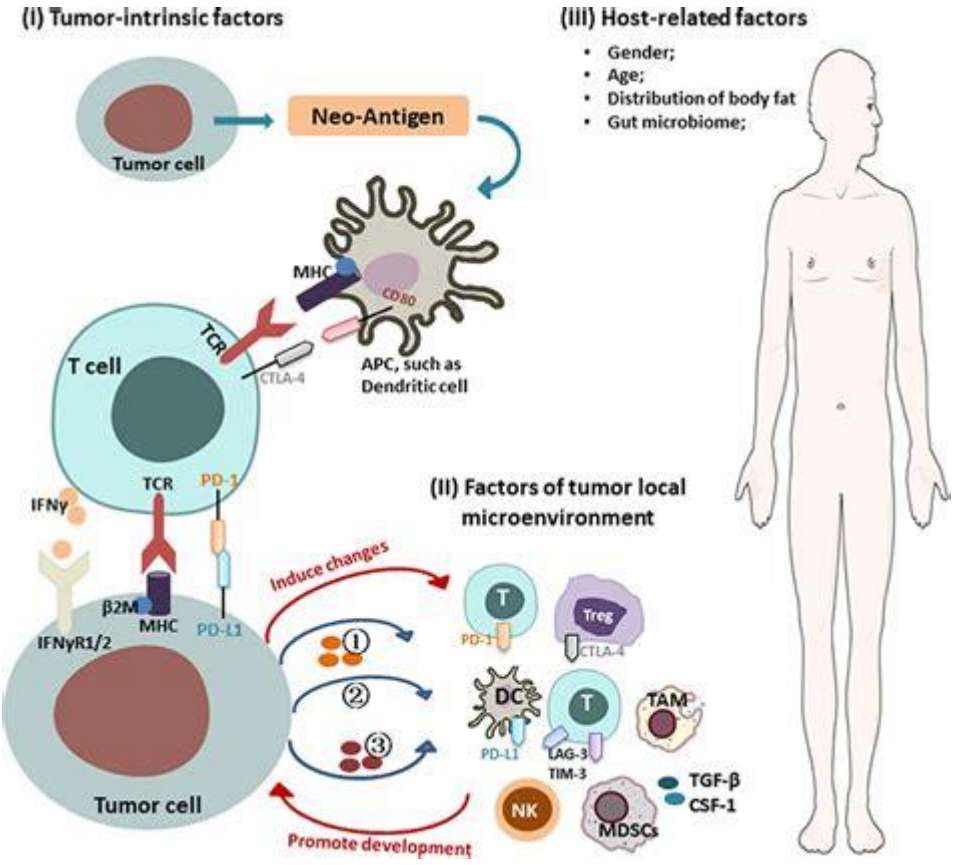

Fig 2: **Mechanisms of Cancer Resistance to Immunotherapy**" by Rilan Bai et al., published in *Frontiers in Oncology* in 2020. This figure visually summarizes the multifaceted mechanisms through which tumors resist immune checkpoint inhibitors (ICIs), categorizing them into tumor-intrinsic factors,

tumor-extrinsic factors, and host-related factors.Bai, R., Chen, N., Li, L., Du, N., Bai, L., Lv, Z., Tian, H., & Cui, J. (2020).

Clinical Applications of Liquid Biopsies

Early Detection and Diagnosis

As a non-invasive alternative to imaging and tissue biopsy, liquid biopsies seem promising for early cancer detection. Liquid biopsies can detect cancer-related genetic changes in asymptomatic or high-risk individuals before clinical signs develop, which is a major benefit. Studies have shown that ctDNA can be found in early-stage cancer patients' blood even when tumours are too tiny to image. Early cancer detection allows for faster interventions and better treatments, improving survival rates.

Recent clinical trials have used liquid biopsies to screen lung cancer. In 2020, JAMA Oncology reported that ctDNA screening in high-risk lung cancer patients detected disease mutations early, enabling early therapies that improved patient outcomes. In colorectal, breast, and ovarian cancers, liquid biopsies may be useful for early screening, especially in hard-to-screen populations [22].

Monitoring Tumor Evolution

Liquid biopsy facilitates real-time monitoring of tumour progression and therapy efficacy. Conventional tissue biopsies capture the tumor's genetic landscape at a specific moment, although they fail to detect dynamic changes. As cancers advance, new mutations, metastasis, and treatment resistance may arise. Liquid biopsy facilitates continuous observation of these changes, disclosing tumour progression throughout therapy [23].

In breast cancer and melanoma, ctDNA analysis monitors tumour mutations and clonal evolution in real time. Nature Medicine published findings on utilising ctDNA to monitor patients with metastatic melanoma during treatment. Alterations in ctDNA levels forecasted disease progression or remission and correlated with tumour response to treatment. By monitoring these alterations through liquid biopsy, clinicians can implement more informed treatment modifications to provide patients with optimal therapy tailored to their tumour profile [24].

Tracking Therapeutic Resistance

A primary clinical application of liquid biopsies is the monitoring of therapy resistance. Chemotherapy, targeted treatments, and immunotherapies reduce tumours; nonetheless, resistance leads to recurrence or disease progression. Clinicians can modify treatment protocols by identifying resistance mutations in real time by liquid biopsy.

Monitoring ctDNA in non-small cell lung cancer exemplifies the role of liquid biopsy in tracking resistance. Secondary mutations, such as the T790M mutation, can render epidermal growth factor receptor (EGFR) therapy ineffective for patients with non-small cell lung cancer (NSCLC). Liquid biopsy can identify this ctDNA mutation, enabling clinicians to transition to a third-generation EGFR inhibitor prior to the manifestation of clinical resistance. Early discovery of resistance mutations enhances patient outcomes by facilitating prompt therapy adjustments to halt disease progression [13,16].

Minimal Residual Disease and Monitoring Metastasis

MRD is the small amount of cancer cells that remain after treatment and might induce relapse. Patients in remission or needing extra treatment are identified by MRD detection. MRD detection requires liquid biopsy in haematologic malignancies like leukaemia, where ctDNA and CTCs can track small quantities of cancer cells in the bloodstream.

The Lancet Oncology examined acute lymphoblastic leukaemia patients for MRD using ctDNA. The study found that rising ctDNA levels required intervention before clinical recurrence. High-risk patients may receive targeted therapy or stem cell transplants before illness recurrence.

In addition to MRD, liquid biopsy can track metastases. Cancer metastasis can be indicated by CTCs or ctDNA in the blood. CTCs follow breast cancer's liver and lung spread. CTCs and ctDNA levels enable clinicians track cancer progression, assess treatment efficacy, and adjust treatment based on metastasis [25].

Liquid biopsy detects early detection, tumour evolution, medication resistance, minimal residual disease, and metastasis, revolutionising cancer care. By providing real-time, non-invasive genetic and molecular insights into cancer, liquid biopsy improves patient outcomes and personalised treatment. Advanced liquid biopsy technology and clinical validation will boost their cancer management stance.

Challenges and Limitations

Sensitivity and Specificity

Clinically, liquid biopsies' sensitivity and specificity for biomarkers such ctDNA and CTCs are problematic. Although promising for cancer identification and medication resistance monitoring, liquid biopsies can be insensitive in early-stage malignancies or patients with low tumour load. Sometimes circulating ctDNA or CTCs are too low to detect. Early-stage cancers or small tumours may release insufficient ctDNA into the bloodstream, reducing liquid biopsy sensitivity. A false positive or negative might misrepresent disease state and lead to unnecessary treatments or missed early intervention.

For pancreatic or glioblastoma, liquid biopsies are less sensitive than lung or colorectal ones. This limitation is especially obvious in mild metastatic activity, where tumor-derived DNA or cells are infrequently discharged. Clinical study attempts to increase liquid biopsy test sensitivity by increasing sequencing depth or CTC separation [26].

Technical and Standardization Issues

Laboratory standardisation hinders liquid biopsy uptake. There is no standard liquid biopsy protocol, hence results vary. Sample collection, processing, DNA extraction, and sequencing vary amongst labs, lowering accuracy and reproducibility. Different ctDNA or CTC separation methods can impact sensitivity, and sequencing or bioinformatics analysis tools can affect data interpretation.

Unharmonised criteria make it difficult to compare study and clinical results. Liquid biopsy is unpredictable, making it challenging to employ clinically and diagnostically. From blood collection to molecular analysis, liquid biopsy workflows are being standardised to ensure consistent results across healthcare settings [26].

Cost and Accessibility

Liquid biopsies are rarely employed in low- and middle-income countries due to the high cost of sequencing technologies like NGS. Specialised equipment and skilled workers are needed to process liquid biopsy samples, increasing costs. Due to liquid biopsy limitations, resource-limited patients may not have access to advanced diagnostic procedures. High sequencing costs limit the number of tests, making routine monitoring or screening problematic, especially for low-detection tumours or remission patients. Make liquid biopsy technologies more affordable and lower sequencing costs to make them more accessible. Cheaper sequencing platforms and easier tumor-derived DNA or cell extraction could solve these issues [22].

Ethical and Regulatory Barriers

Ethical and regulatory difficulties with liquid biopsy include genetic data privacy and test regulation. Privacy, consent, and usage issues arise when liquid biopsies show a person's genetic vulnerability to cancer and other diseases. Patients' genetic data must be securely stored, communicated, and used ethically for liquid biopsies to become common.

The FDA and EMA challenge fluid biopsy tests. Clinical validation ensures the accuracy, reliability, and clinical usefulness of regulatory-certified liquid biopsy assays. The lack of regulatory frameworks for liquid biopsies makes clinical use problematic.

In conclusion, liquid biopsies can diagnose, monitor, and treat cancer, but their sensitivity, standardisation, cost, and regulatory approval must be addressed. These restrictions must be solved by research, technology, and global collaboration to make liquid biopsies accessible, reliable, and standardised cancer tools [13,27].

Future Directions

Technological Advancements

NGS, CRISPR, and AI-driven analysis will shape liquid biopsies. By detecting even modest amounts of ctDNA, NGS has enhanced liquid biopsy sensitivity and depth, enabling earlier detection and more precise cancer evolution tracking. Liquid biopsies can detect more tumours and track resistance mechanisms as sequencing technology improves in speed, affordability, and accuracy.

CRISPR-based technologies, however new, could increase liquid biopsies' sensitivity and specificity. CRISPR may accurately change and enrich target DNA sequences, making medication resistance or minimal residual disease mutations easier to find. This method may boost sensitivity in low-tumor cases.

AI and ML for liquid biopsy data analysis is another intriguing improvement. AI algorithms can find complex patterns and subtle changes in vast sequencing and imaging datasets that people miss. AI-driven analysis could customise care, improve treatment, and discover cancer biomarkers [28].

Integration with Other Diagnostics

As a standalone diagnostic tool, liquid biopsy is promising, but combining it with additional methods could improve cancer surveillance. More accurate cancer diagnosis may result from liquid biopsy and MRI, CT, and PET scans. Imaging shows tumour size and location, while liquid biopsy shows evolution, metastasis, and treatment resistance. This multi-modal

strategy may improve clinician decision-making and patient outcomes.

In confusing or difficult tissue biopsy results, combining liquid biopsy with normal biopsies may increase therapeutic usage. These technologies could validate liquid biopsy's genetic mutations and clinical relevance, confirming its place in personalised medicine [29].

Global Implementation and Cost Reduction

Making liquid biopsies more economical and accessible worldwide, especially in resource-limited settings, is crucial for their wider use. Increasing tumour marker detection efficiency and lowering sequencing costs will make liquid biopsy a realistic alternative for patients worldwide. Governments, academic institutions, and industry leaders are working together to cut liquid biopsy test costs and develop low-cost alternatives for usage in various healthcare settings.

The introduction of liquid biopsy technology to disadvantaged people in low- and middle-income nations could revolutionise diagnostics. Simplifying sample collection and developing portable, point-of-care liquid biopsy analysis equipment could lower costs and enable global implementation. These developments could democratise cancer care by providing early detection and continuous monitoring through liquid biopsies in all locations [30].

Liquid biopsy's future lies in developing more sensitive technologies, integrating complementing diagnostic procedures, and lowering prices and increasing accessibility worldwide. As these advances continue, liquid biopsy will become increasingly important in cancer detection, monitoring, and therapy worldwide.

Conclusion

Real-time liquid biopsies can track cancer progression and medication resistance, revolutionising oncology. Liquid biopsies assess cancer progression, determine minimum residual sickness, and change treatment options using biomarkers such ctDNA, CTCs, and exosomes. Early-stage cancer detection and therapy response monitoring are substantial advances over standard diagnostics.

Liquid biopsies could transform cancer treatment by offering more tailored and accurate options. Liquid biopsies can detect genetic mutations and track cancer changes, enabling earlier detection, better metastatic monitoring, and speedier treatment. These innovations offer patient-centered, flexible care.

Clinical validation and incorporation into clinical practice are liquid biopsies' future. As technology advances and costs fall, liquid biopsies will shape cancer diagnosis, monitoring, and treatment worldwide.

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Original Article

Diagnostic Efficiency of Ultrasound Imaging in Assessing the Extent of Lymphoma

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Abstract:

Summary: The article presents the results of evaluating the diagnostic efficiency of ultrasound (US) in determining the extent of pathological processes in lymphoma patients. The study included 48 patients with Hodgkin's and non-Hodgkin's lymphoma who were hospitalized at the National Scientific Oncology Center from 2021 to 2024. All participants underwent comprehensive ultrasound of the abdominal parenchymal organs and lymph nodes using B-mode and Doppler imaging. The obtained data indicate high sensitivity and specificity of US in detecting liver, spleen, and abdominal lymph node involvement. Characteristic echographic signs of lymphatic conglomerates and associated complications such as ascites and exudative pleuritis were noted. Given the availability and safety of the method, US can be considered a key tool for primary diagnosis and lymphoma monitoring in clinical practice.

The purpose of the study: To evaluate the diagnostic efficiency of ultrasound (US) in assessing the extent of the disease in lymphoma.

Methods: A retrospective analysis of 48 medical records of patients with confirmed diagnoses of Hodgkin's lymphoma (HL) and non-Hodgkin's malignant lymphoma (NHL) who were treated at the National Scientific Oncology Center between 2021 and 2024. All patients underwent comprehensive abdominal ultrasound, pleural ultrasound, and lymph node imaging with Doppler.

Results: Pathological changes in lymph nodes, spleen, liver, and pleura were detected in all patients. In 60% of cases, the lymph node conglomerates appeared echonegative, while 5% showed signs of aggressive progression (undefined capsules, liquefaction). Typical echographic signs of diffuse and focal organ changes were observed.

Keywords: Lymphoma; Ultrasound; Extent; Diagnosis; Imaging

Introduction

Lymphomas are malignant neoplasms of the lymphatic system that include Hodgkin lymphoma and non-Hodgkin lymphomas. Accurate staging is critical for treatment selection and prognosis. Computed tomography (CT) and positron emission tomography with CT (PET-CT) are established modalities for assessing disease extent; however, they are associated with high cost and exposure to ionizing radiation. Ultrasound (US) remains an accessible, noninvasive, radiation-free technique. The present study aims to evaluate the diagnostic value of US in determining the extent of lymphoma involvement. Lymphomas constitute a complex group of lymphoid tumors occurring across all age groups, and the probability of disease increases with age [1].

Lymphomas are primary neoplasms of lymphoid tissue, belong to tumors of the immune system, and typically arise from lymph nodes. They are divided into two major categories: Hodgkin disease (Hodgkin lymphoma) and malignant non-Hodgkin lymphomas. Among all lymphomas, Hodgkin disease accounts for 25–30% of cases [3].

Non-Hodgkin lymphomas frequently (15.0%–35.0%) present with involvement of lymph nodes, lungs, pleura, pericardium, and other thoracic organs. A variety of high-information imaging methods—CT and magnetic resonance imaging (MRI)—are used for their evaluation; however, owing to cost and limited availability, ultrasonography is often the most practical option.

Relevance

Lymphomas represent a heterogeneous group of malignant disorders of the lymphatic system that require precise diagnosis and staging to guide optimal management. Ultrasonography is a noninvasive, accessible, and highly informative imaging modality that can play a key role in assessing the extent of lymphoma involvement. This article examines the diagnostic performance of US compared with other imaging techniques (CT, MRI, PET-CT) in lymphoma, with particular attention to the potential of ultrasound elastography and Doppler assessment in the differential diagnosis of lymphadenopathy.

Materials and Methods

A retrospective analysis was conducted of 48 medical records of inpatients with diagnoses of Hodgkin malignant lymphoma (HL) and non-Hodgkin malignant lymphoma (NHL) treated at the National Research Oncology Center (JSC “NROC”) during 2021–2024. Patient age ranged from 16 to 69 years. All patients underwent ultrasonography (US) of the liver, spleen, pancreas, kidneys, and adrenal glands with assessment of organ size and echotexture. The retroperitoneal space was carefully examined to identify enlarged lymph nodes, and the chest was assessed to verify exudative pleuritis (exudative pleural effusion).

The following US criteria were used to characterize abdominal lymph node involvement: location, number, size, margins, and degree of echogenicity. Using Doppler ultrasonography, qualitative hemodynamic features were evaluated in affected lymph nodes, including flow pattern (central, peripheral, or mixed) and flow intensity, determined by the number of color Doppler signal foci (intense, low-intensity, or moderately intense).

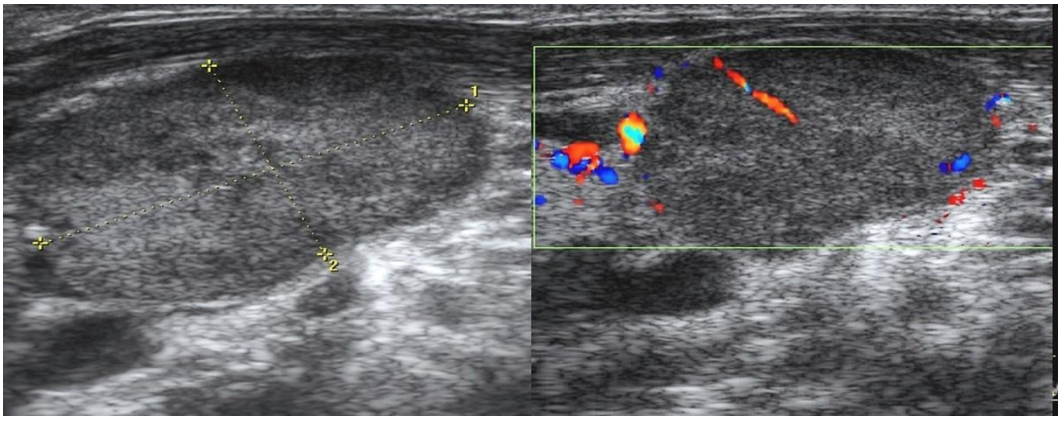
Results

Hepatomegaly was identified in all patients (100%). Based on hepatic echotexture, diffuse changes were observed in 20 cases (41.6%), focal changes in 8 cases (16.8%), and combined diffuse–focal changes in 20 cases (41.6%). Diffuse changes were characterized on sonograms by homogeneous darkening of the organ with blurring of the hepatic architecture. Focal changes appeared as solitary and scattered hypoechoic foci without well-defined margins; hyperechoic foci were interpreted as fibrotic areas, and anechoic zones as areas of liquefaction. Combined diffuse–focal changes presented as alternating hyper- and hypoechoic foci against a background of diffusely reduced echogenicity.

All patients also demonstrated enlargement of intra-abdominal lymph nodes (100%). Nodes were arranged in groups along major vessels (aorta, inferior vena cava, and iliac vessels), often forming “packs” or large conglomerates, and clustered at the hepatic, splenic, and renal hila. On sonograms, lymph nodes appeared as oval or round structures of reduced echogenicity. In 60% of cases they presented as echonegative (hypoechoic) with smooth, well-defined margins. The nodal capsule was visualized as an

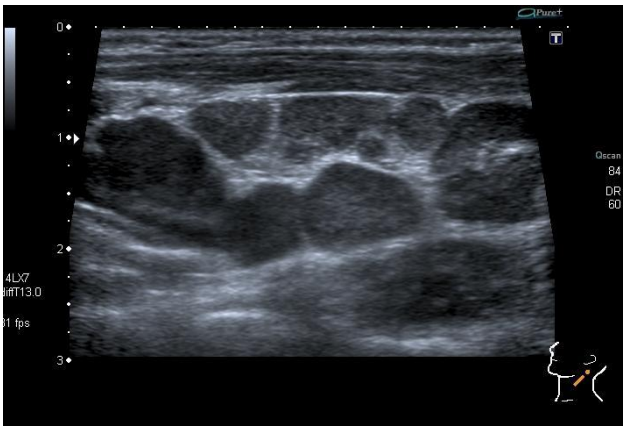
echogenic line, which was not always sharply delineated.

Figure 1. Hypoechoic heterogeneous structure of a lymph node.



In some patients (5%), lymph nodes were in very close apposition to one another. Large conglomerates exhibited heterogeneous echotexture. An echogenic capsule could be traced along the outer contour of the conglomerate and between individual nodes; in some large conglomerates the capsule was only partially visible or entirely absent. The conglomerate appeared as a tumor-like mass with a lobulated surface or with areas of liquefaction.

Figure 2. Conglomerate of lymph nodes in the submandibular region.



Differentiating individual nodes within such a conglomerate was not always feasible. Large conglomerates in which separate lymph nodes and their capsules cannot be clearly delineated typically indicate an aggressive disease course with spread to adjacent structures, consistent with published data [5].

Large conglomerates led to noticeable displacement and compression of abdominal vessels, the stomach, intestines, and urinary bladder. Edema of the limb was observed on the side of pronounced lymphadenopathy located in the iliac region and the lesser pelvis. In lymphomas, involvement of other organs and tissues—either primary or secondary—is not uncommon, particularly of the gastrointestinal tract, lungs and pleura, pericardium, kidneys, and mammary glands. Our observations corroborate reports that malignant lymphomas of the stomach and intestine account for 0.5% of all gastrointestinal malignancies [2,4].

In our data set, sonography most clearly enabled verification of intestinal tumor involvement. On echograms, intestinal lymphoma appeared as a heterogeneous mass of varying size with ill-defined margins, characterized by a hypoechoic periphery and an echogenic center.

Ultrasound of the pancreas revealed no specific changes; only an age-related increase in echogenicity was noted. No specific renal parenchymal involvement was identified, although kidney size was increased. The parenchyma of solid organs was sonographically characterized by reduced echogenicity. In patients with renal involvement, enlarged lymph nodes were often recorded adjacent to the organs.

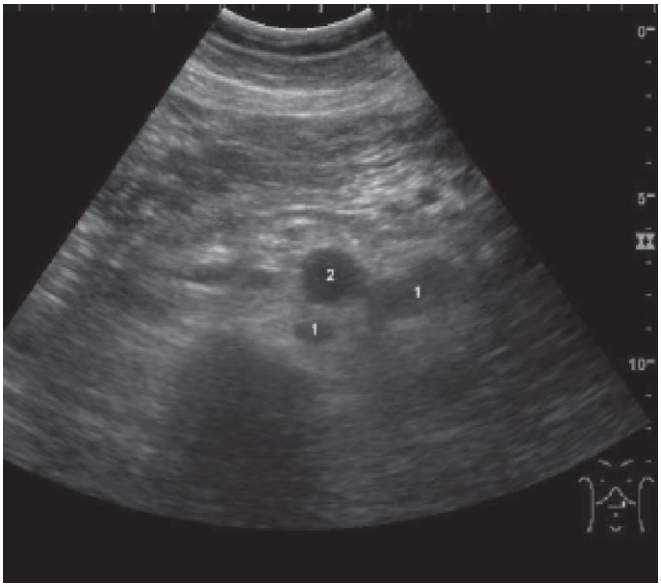
In both NHL and HL, the pleura may be involved in the tumor process. Primary pleural involvement is rare; however, with disease generalization or relapse, the probability increases [1,5]. In view of this, we performed 91 ultrasound examinations of the pleural cavities. A characteristic finding was fluid accumulation within the pleural spaces. Sonography reliably detects pleural effusion; the sonographic hallmark is an anechoic space surrounding the lung parenchyma, either bilaterally or unilaterally.

Occasionally, abdominal ultrasound revealed ascitic fluid, which appears on the monitor as an

anechoic structure. We observed three patients with free intraperitoneal fluid.

Discussion

In summary, ultrasonography is a valuable diagnostic modality for HL and NHL. Its high informativeness supports recommending it as one of the principal methods for establishing involvement of abdominal lymph nodes and parenchymal organs in lymphoma. When lymphadenopathy is detected, a systematic assessment of the liver, spleen, and other organs is essential. Affected lymph nodes are most commonly situated along major vessels (para-aortic, paracaval, along the iliac vessels) and at organ hila (liver, spleen, kidneys). At stages III and IV, enlargement of abdominal and retroperitoneal lymph nodes was consistently observed.



Hepatic and splenic involvement is quite common in both NHL and HL. In diffuse lesions of the spleen and liver, overall echogenicity is reduced. The sonographic appearance of focal lesions in the liver and spleen is similar: foci with depleted internal echoes. Small foci are more often hypoechoic, whereas larger ones are heterogeneous with areas of liquefaction or calcification.

Ultrasonography also provides important diagnostic information for other extranodal sites, including the gastrointestinal tract, pleura, kidneys, and adrenal glands. Involvement of these organs is observed less frequently and more often in the setting of prolonged disease, biologic aggressiveness, or relapse. Detection by US of splenomegaly and enlarged abdominal lymph nodes may indicate the need to continue chemotherapy and, not infrequently, support consideration of additional local radiotherapy to the involved nodal regions.

Conclusion

This study demonstrated the high diagnostic effectiveness of ultrasonography (US) for assessing the extent of disease in lymphoma. US performed well in detecting involvement of lymph nodes, liver, spleen, and other parenchymal organs, as well as in identifying characteristic sonographic signs of complications such as ascites and exudative pleural effusion. The method shows high sensitivity and specificity, making it a valuable tool for initial diagnosis and monitoring of lymphomas—particularly where access to more expensive, resource-intensive modalities such as CT and MRI is limited.

In addition, the combined use of B-mode and Doppler ultrasonography substantially improves diagnostic accuracy, enabling not only assessment of nodal involvement but also evaluation of vascular invasion, which is critical for therapeutic decision-making. Given its accessibility, safety, and noninvasiveness, ultrasonography can be recommended for broad application in clinical practice, especially in resource-constrained settings.

Thus, ultrasound imaging is an important component of the diagnostic and follow-up toolkit for patients with lymphoma, facilitating earlier detection and timely intervention.

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Author Contributions: Orazbayeva D. was responsible for data collection. Nurbek Zh. was responsible for statistical data processing. Isa G. was responsible for the article concept.

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Ethics approval: none

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Case Report

Combined Endoscopic Treatment of Gastric Arterio-Venous Malformation

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Abstract:

Gastric antral vascular ectasia (GAVE), also known as "watermelon stomach," is a rare but clinically significant cause of chronic anemia and upper gastrointestinal bleeding, particularly in elderly patients. Although uncommon, GAVE considerably affects quality of life due to recurrent bleeding, frequent hospitalizations, and the need for blood transfusions. Diagnosis is typically based on endoscopic findings, characterized by red, radiating streaks from the pylorus or multiple punctate angioectasias in the antrum. Therapeutic approaches include various endoscopic methods, most notably argon plasma coagulation (APC) and endoscopic band ligation (EBL), each with specific advantages and limitations. Recent studies have emphasized the benefits of combining these two modalities to achieve more effective and durable hemostasis.

This case report presents a 79-year-old female patient with GAVE syndrome, manifested by chronic iron-deficiency anemia. Initially, the patient underwent APC, which provided temporary improvement but failed to achieve complete resolution. On follow-up endoscopy, persistent angioectatic lesions prompted a second-stage procedure using a combined treatment strategy: three elastic bands were applied to the most prominent vascular areas, followed by APC on residual superficial lesions. Over the next three months, the patient underwent regular endoscopic surveillance and laboratory monitoring. Follow-up assessments revealed significant clinical and endoscopic improvement, including normalization of hemoglobin levels and regression of vascular malformations, with no signs of recurrent anemia or bleeding.

This clinical case highlights the effectiveness and safety of combined endoscopic therapy using EBL and APC in patients with refractory or recurrent GAVE. The synergistic action of both techniques allows for comprehensive treatment of both superficial and deeper vascular lesions, improving long-term outcomes and reducing the need for repeated interventions. Combined therapy may be considered the treatment of choice in complex GAVE cases, offering a promising strategy in routine endoscopic practice.

Keywords: Gastric Antral Vascular Ectasia; Chronic Anemia; Endoscopy; Gastrointestinal Bleeding; Argon Plasma Coagulation

Introduction

Gastrointestinal bleeding (GIB) is one of the leading causes of emergency hospitalization and remains a pressing issue in clinical gastroenterology. Among non-variceal sources of bleeding, gastric antral vascular ectasia (GAVE syndrome) is a rare yet clinically significant condition that predominantly affects older adults. According to various authors, GAVE accounts for approximately 4% of all non-variceal upper gastrointestinal hemorrhages [1].

GAVE may present with episodes of acute blood loss or as chronic iron-deficiency anemia with positive fecal occult blood testing. This condition substantially impairs patients' quality of life and increases the need for repeat hospitalizations and blood transfusions [2].

The typical endoscopic appearance includes red streaks radiating from the pylorus (the "watermelon stomach" sign) or multiple punctate angioectasias creating a "honeycomb" pattern. The diagnosis is confirmed by esophagogastroduodenoscopy (EGD), and in uncertain cases by histology demonstrating vascular ectasia, thrombosis, spindle-cell proliferation, and fibro-hyalinosis.

Several endoscopic modalities are used in the treatment of GAVE. Argon plasma coagulation (APC) is the most common technique for ablating superficial vessels. An alternative is endoscopic band ligation (EBL), which can effectively target deeper vessels. In recent years, combined EBL and APC has been actively discussed as a strategy to achieve more durable hemostasis and reduce recurrence rates [3].

Case Report

Patient K., born in 1945, presented with chronic anemia and chronic erosive gastritis and was referred for EGD prior to elective coronary angiography. At the first examination, the endoscopist interpreted GAVE as distal erosive gastropathy. At a follow-up examination on September 1, 2025 (note: this date precedes subsequent 2024 events in the timeline and may require correction), after treatment for gastric erosions, another endoscopist diagnosed arteriovenous malformation of the antrum ("watermelon stomach," i.e., GAVE syndrome) based on the characteristic macroscopic appearance (Fig. 1).

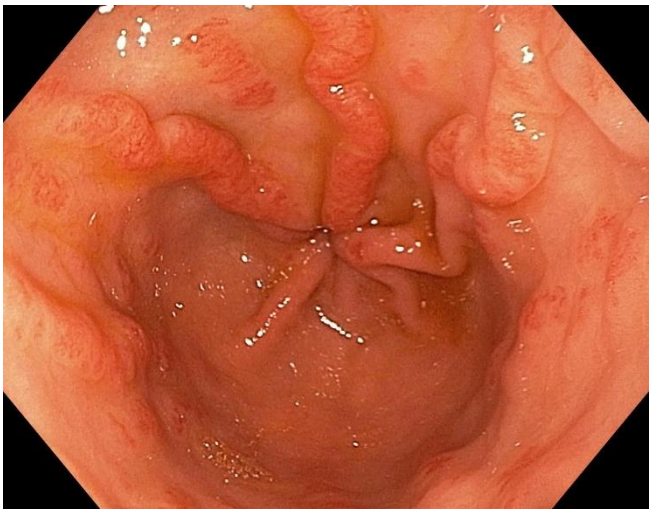


Figure 1. Endoscopic appearance of an arteriovenous malformation of the stomach ("watermelon stomach," GAVE syndrome).

On September 19, 2024, the patient was electively admitted with a diagnosis of GAVE syndrome to the Surgical Department of the National Research Oncology Center (NROC). On admission, the complete blood count dated September 13, 2024 showed: leukocytes 4.8 g/L, hemoglobin 98 g/L, platelets 243 g/L, erythrocytes 3.5 g/L, hematocrit 37.4%, ESR 27 mm/h.

On September 20, 2024, APC of gastric vascular malformations was performed. On September 23, 2024, the patient was discharged in satisfactory condition with a recommendation for repeat endoscopy in one month.

Exactly one month later, on October 21, 2024, a control EGD was performed at the patient's local clinic, revealing multiple gastric erosions and ulcers; treatment by a gastroenterologist was recommended.

On November 17, 2024, a further control EGD demonstrated small foci of angioectasia in the pyloric canal, decreased in number compared with prior examinations. A second-stage inpatient treatment for angioectasias at NROC was recommended.

On December 4, 2024, the patient was electively re-admitted to the Surgical Department of NROC. On admission, the CBC dated November 26, 2024 showed: hemoglobin 103 g/L, leukocytes 4.67/L, erythrocytes 3.76/L, platelets 192/L, ESR 15 mm/h. On December 5, 2024, combined endoscopic treatment of arteriovenous malformations of the antral mucosa was performed: three ligating bands were applied to mucosal areas with angioectasias, followed by APC of the remaining abnormal zones (Fig. 2). On December 9, 2024, the patient was discharged in satisfactory condition.

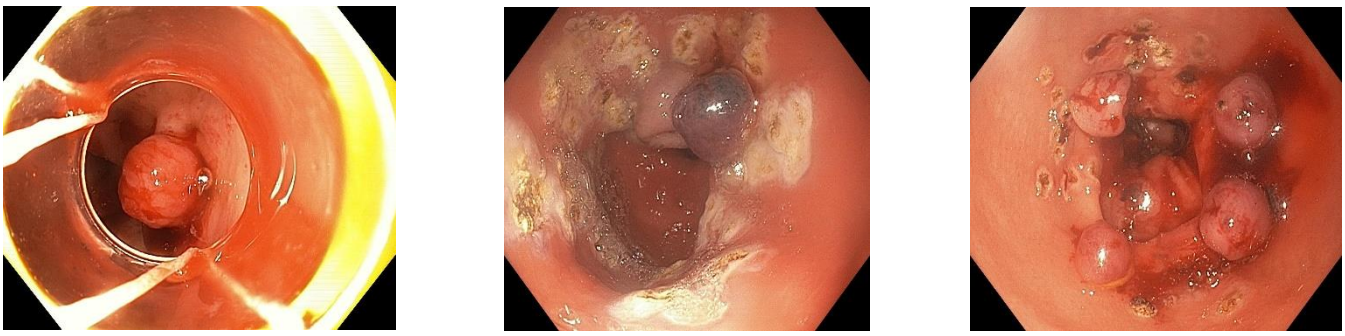
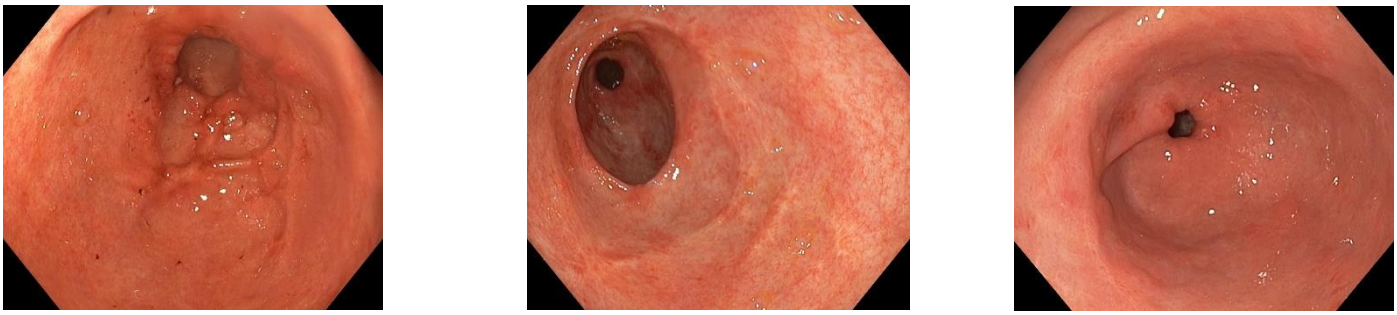


Figure 2. Steps of endoscopic band ligation and argon plasma coagulation for arteriovenous malformations of the gastric mucosa.

On January 5, 2025, a control EGD showed the following endoscopic findings: the distal gastric mucosa was smooth, pale, atrophic, with numerous small flat erosions; residual foci of mucosa with arteriovenous malformations were visualized; four ulcerative defects measuring 0.4 × 0.3 cm were identified in the pyloric canal, with fibrin-covered bases after prior endoscopic ligation (Fig. 3a).

At follow-up on March 11, 2025, flat, stellate scars were observed at the sites of prior ulcers, with a few pale angioectatic foci in the pyloric canal (Fig. 3b). The CBC dated March 9, 2025 showed: hemoglobin 129 g/L, leukocytes 4.5/L, erythrocytes 3.8/L, platelets 220/L, ESR 10 mm/h.

On March 30, 2025, serial control EGD revealed delicate scarring of the distal gastric mucosa without overt vascular malformations (Fig. 3c).



a b c

Figure 3. Endoscopic findings over time: (a) one month after combined endoscopic therapy; (b) two months after therapy; (c) three months after therapy.

Based on serial EGD and laboratory results, dynamic observation was recommended. Over three months of follow-up, no evidence of anemia was detected. The course of the disease is summarized in Table 1.

Discussion

Endoscopic ligation (EL) operates on the principle of applying elastic bands to pathologically altered vessels. This induces mechanical compression, ischemia, and subsequent replacement by fibrous tissue. The method specifically targets deeper vascular structures, which can be the source of recurrent bleeding. Literature data suggest a lower recurrence rate with EL compared to argon plasma coagulation (APC), as well as a reduced need for repeat procedures.

Nevertheless, EL has certain technical limitations. In some instances, the antral gastric mucosa cannot be adequately drawn into the ligator cap, especially in cases of pronounced scarring or atrophy, which can diminish the method's effectiveness [4].

Argon plasma coagulation (APC) remains a convenient and safe method for superficial vascular ablation, allowing for the treatment of broad areas of affected mucosa. However, in some cases, particularly with deep or recurrent lesions, the effectiveness of APC is limited.

The combined application of EL and APC allows for overcoming the limitations of each method due to their complementary actions. EL addresses deep angioectasias, while APC targets superficial lesions. According to modern meta-analyses, this combined

approach yields more stable clinical outcomes, reduces the need for blood transfusions, and decreases the number of repeat interventions [5].

Table 1. Clinical timeline of the case

Date	Event	Notes
01.09.2025	Elective follow-up gastroscopy (EGD) after gastroenterologist-directed therapy for gastric erosions	Initial diagnosis of arteriovenous malformations of the stomach (watermelon stomach, GAVE syndrome) based on characteristic endoscopic appearance.
13.09.2024	Complete blood count (CBC) Leukocytes 4.8 g/L, hemoglobin 98 g/L, platelets 243 g/L, erythrocytes 3.5 g/L, hematocrit 37.4%, ESR 27 mm/h.	Findings support anemia.
19.09.2024	Elective admission to the Surgical Department, National Research Oncology Center (NROC)	Baseline assessment and planning of endoscopic therapy.
20.09.2024	Argon plasma coagulation (APC) of gastric vascular malformations	APC of arteriovenous malformations of the antral mucosa, Soft Coagulation mode, 50 W.
23.09.2024	Discharged in satisfactory condition.	Follow-up gastroscopy is recommended in one month.
21.10.2024	A control gastroscopy was performed at the patient's local municipal polyclinic.	During this procedure, the endoscopist identified multiple erosions and gastric ulcers, leading to a recommendation for gastroenterological consultation and treatment.
17.11.2024	Control Gastroscopy	During a subsequent gastroscopy, minor foci of angioectasias were observed in the pyloric canal region, showing a dynamic reduction in their number. A second stage of treatment for the angioectasias was recommended for inpatient management at the NROC
26.11.2024	Complete Blood Count (CBC)	Hemoglobin: 103 g/L White Blood Cells (WBC): 4.67/L Red Blood Cells (RBC): 3.76/L Platelets: 192/L Erythrocyte Sedimentation Rate (ESR): 15 mm/h
04.12.2024	Planned hospitalization in the surgical department of the NROC	Was arranged for endoscopic treatment
05.12.2024	Combined treatment for arteriovenous malformations of the gastric antrum was performed as planned.	This involved the application of three ligating bands to the mucosal areas with angioectasias, followed by argon plasma coagulation of the remaining altered areas.
09.12.2024	Discharge from Hospital	The patient was discharged in satisfactory condition
05.01.2025	Control Gastroscopy	A control gastroscopy revealed the following endoscopic findings: The mucosa in the distal regions was smooth, pale, atrophic, with numerous small, flat erosions. Foci of mucosal arteriovenous malformations were visualized. Within the pyloric canal, four ulcerative defects, measuring 0.4x0.3 cm, were identified; their bases were filled with fibrin following the previously performed endoscopic ligation.
09.03.2024	Complete Blood Count	Hemoglobin: 129 g/L White Blood Cells (WBC): 4.5/L Red Blood Cells (RBC): 3.8/L Platelets: 220/L (ESR): 10 mm/h
11.03.2024	Control Gastroscopy	During a follow-up examination on March 11, 2025, flat, stellate scars were noted at the sites of the ulcerative defects, with isolated, pale foci of angioectasias in the pyloric canal area.
30.03.2025	Control Gastroscopy	The mucosal lining presented with delicate mucosal scars in the distal segments, without clearly expressed foci of vascular malformations.
From March 11 to Present	Dynamic observation continues at the patient's place of residence.	The patient's overall condition remains unaffected, with no evidence of anemia.

Conclusion

Gastric Antral Vascular Ectasia (GAVE) syndrome is a rare but clinically significant condition associated with chronic anemia and the risk of recurrent bleeding. Endoscopic treatment utilizing both APC and EL is an effective therapeutic tool for this condition. The combination of EL and APC provides a more comprehensive approach to vascular changes, thereby improving clinical outcomes. The presented clinical case demonstrates the high efficacy of this combined approach and confirms its utility in the management of recurrent GAVE. The combined methodology can be recommended as a preferred approach for treating complex and resistant forms of GAVE.

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Case Report

Hodgkin's Lymphoma as a Rare Variant of Richter's Syndrome in Chronic Lymphocytic Leukemia: A Clinical Case Description

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Abstract:
Richter's syndrome (RS) is a malignant transformation of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) into a more aggressive lymphoid neoplasm. Typically, this term refers to the development of diffuse large B-cell lymphoma (DLBCL), which accounts for 90-95% of transformations. Much more rarely (in less than 5% of cases), the so-called Hodgkin's variant of Richter's syndrome occurs—transformation into classical Hodgkin's lymphoma (HL). [1] The Hodgkin's variant is characterized by the appearance of Reed-Sternberg cells or their variants in the infiltrate, surrounded by an inflammatory background typical of HL. It most often develops in patients with a long history of CLL/SLL, sometimes in the context of immunosuppression or after treatment with purine analogs and monoclonal antibodies. [2] The clinical picture of the Hodgkin's variant of Richter's syndrome typically includes pronounced B-symptoms (fever, night sweats, weight loss), rapidly progressing enlargement of lymph nodes and/or splenomegaly. Unlike the DLBCL variant, the course may be somewhat less aggressive; however, the prognosis remains unfavorable compared to primary Hodgkin's lymphoma. [3]

Keywords: Chronic Lymphocytic Leukemia (CLL); Hodgkin's Lymphoma; Richter's Transformation; Venetoclax; Bruton Tyrosine Kinase Inhibitors (BTK Inhibitors); BV-AVD

Introduction

Richter's syndrome (RS) is a malignant transformation of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) into a more aggressive lymphoid neoplasm. Typically, this term refers to the development of diffuse large B-cell lymphoma (DLBCL), which accounts for 90-95% of transformations. Much more rarely (in less than 5% of cases), the so-called Hodgkin's variant of Richter's syndrome occurs—transformation into classical Hodgkin's lymphoma (HL). [1]

The Hodgkin's variant is characterized by the appearance of Reed-Sternberg cells or their variants in the infiltrate, surrounded by an inflammatory background typical of HL. It most often develops in patients with a long history of CLL/SLL, sometimes in the context of immunosuppression or after treatment with purine analogs and monoclonal antibodies. [2]

The clinical picture of the Hodgkin's variant of Richter's syndrome typically includes pronounced B-symptoms (fever, night sweats, weight loss), rapidly progressing enlargement of lymph nodes and/or splenomegaly. Unlike the DLBCL variant, the course may be somewhat less aggressive; however, the prognosis remains unfavorable compared to primary Hodgkin's lymphoma. [3]

Diagnosis is confirmed through histological and immunohistochemical examination of the lymph node biopsy or affected organ. Treatment involves chemotherapy regimens typically used for Hodgkin's lymphoma (ABVD, BEACOPP, etc.), often combined with antiviral or targeted therapy. In cases of resistant forms, autologous or allogeneic hematopoietic stem cell transplantation may be considered. [3] [4]

This clinical case illustrates the rare variant of Richter's syndrome with transformation into Hodgkin's lymphoma, demonstrating the challenges in diagnosis, differential assessment of morphological changes, and the choice of optimal treatment strategy for patients with CLL.

Clinical Case

Patient M., born in 1958, has been under observation since 2009 for chronic lymphocytic leukemia, diagnosed based on morphological, immunological, and clinical-hematological data. During the observation, several lines of therapy were administered, including:

- Chemotherapy with FC and RFC regimens;
- Monoclonal immunotherapy with rituximab;
- Since 2020—targeted therapy with Bruton's tyrosine kinase inhibitor (ibrutinib 420 mg/day) due to the presence of deletion 17p13 (del(17p)).

On the background of ibrutinib therapy, stable disease control was achieved. However, in the spring of 2025, the patient showed clinical and laboratory deterioration: enlargement of peripheral lymph nodes (right axillary lymph nodes up to 2.6×1.3 cm, 1.4×0.5 cm, and 1.2×0.5 cm, left up to 1.2×0.6 cm, 1.6×0.5 cm; inguinal lymph nodes: right up to 1.3×0.3 cm, 0.6×0.4 cm, 1.1×0.4 cm, left up to 1.2×0.4 cm, 1.4×0.4 cm), increase in lymphocytosis, appearance of B-symptoms (night sweats, low-grade fever), as well as splenomegaly.

The patient was admitted to the LLP "National Scientific Oncology Center" in the Department of Lymphoproliferative Diseases, where on April 16, 2025, an excision of the left axillary lymph node was performed to exclude Richter's transformation. Given the disease progression, combined therapy was started: venetoclax (BCL-2 inhibitor) in combination with continued ibrutinib therapy.

Diagnosis of Transformation

Histological and immunohistochemical examination confirmed the diagnosis of Richter's transformation into classical Hodgkin's lymphoma (CHL-RT). The histological report showed a picture of a B-cell lymphoma of small lymphocytes (CLL/SLL) with areas morphologically resembling classical Hodgkin's lymphoma, containing Hodgkin and Reed-Berezovsky-Sternberg (RB-S) cells.

Immunohistochemically, small cells expressed CD20, PAX5, CD5, and CD23, while large Hodgkin-type cells were positive for CD30 and PAX5 but negative for CD20. These findings confirmed the diagnosis of CLL/SLL transformed into Hodgkin's lymphoma.

Due to the rarity of Hodgkin-like transformation, the material was sent for a second opinion to the reference laboratory of the Federal State Budgetary Institution "NMIC Hematology" of the Ministry of Health of the Russian Federation, Moscow, where the conclusion was confirmed. The results of the secondary examination: the morphological picture of the lymph node is characterized by a focal-diffuse lymphoid infiltrate of small cells with signs of proliferative activity and areas of fibrous tissue containing Hodgkin and Reed-Berezovsky-Sternberg cells.

Treatment

Venetoclax therapy is effective against CLL but does not affect Hodgkin's lymphoma cells. Considering the presence of a dual hematologic substrate (CLL and CHL-RT), the possibility of adding chemotherapy with the BV-AVD regimen (brentuximab vedotin + doxorubicin, vinblastine, dacarbazine) [2,3] was considered.

Unfortunately, PET-CT was not performed before the start of treatment due to limitations in the availability of this procedure and the rapid progression of the disease.

Given the aggressive course of the disease, a decision was made to begin combined therapy with venetoclax + BV-AVD as a potentially effective option. Ibrutinib was discontinued after escalating the dose of venetoclax within the planned regimen.

From June 13 to June 27, 2025, the first course of the regimen was administered. No complications were noted during hospitalization. A repeat course of BV-AVD is planned, after which treatment efficacy will be evaluated using PET-CT.

Discussion

Richter's syndrome (RS) is the transformation of CLL into a more aggressive malignant disease, characterized by rapid progression and often limited response to treatment. The key method for diagnosing RS is histopathological examination. The most common form of RS is DLBCL, found in 2-8% of patients with CLL. However, other transformation variants are described in the literature, including T-cell lymphomas, multiple myeloma, Burkitt lymphoma, and lymphoblastic lymphoma.

The Hodgkin's variant of transformation occurs in less than 1% of RS cases. To date, about 100 confirmed observations of CHL-RT have been published in the literature. Two histological types of HL in CHL-RT are distinguished:

- Type I—Reed-Sternberg cells are scattered or grouped against the typical CLL infiltrate background.
- Type II—Reed-Sternberg cells are found on a polymorphic reactive background, making the picture indistinguishable from de novo Hodgkin's lymphoma.

The most common histological subtype of HVRT is the mixed-cell variant, followed by nodular sclerosis, lymphocytic depletion, and lymphocytic predominance. [5–8]

Our clinical case corresponds to Type I: in several sections of the small-cell lymphoid infiltrate, nodular-like structures with stromal fibrosis are identified, represented by small lymphoid cells, fibroblasts, histiocytes, and plasma cells. Among them, individual large Hodgkin and Reed-Sternberg cells are detected.

Despite the availability of various chemotherapy regimens, the treatment of CHL-RT remains a challenging task, and the prognosis is worse than for primary Hodgkin's lymphoma. Literature describes combined regimens directed at HL: ABVD, BEACOPP, CHOP ± R, CVPP [7–9]. Patients achieving complete remission remain under observation until disease progression; in the absence of complete remission, regimens for refractory HL are considered, as well as the possibility of non-myeloablative allogeneic hematopoietic stem cell transplantation in the first remission.

Promising therapy directions include the use of anti-EBV agents and monoclonal antibodies against CD30 (brentuximab vedotin), but the results are still limited. Overall, the response to treatment and clinical outcomes in CHL-RT are worse than for de novo HL but better than for the DLBCL variant of RS.

In our case, the patient tolerated the first course of chemotherapy well, feels good, and remains under observation until the second course is completed, after which treatment response will be evaluated.

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